Association of inflammation markers with epicardial adipose tissue in drug naive metabolic syndrome

Inflammation markers in metabolic syndrome

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Abstract

The metabolic syndrome (MetS) or syndrome X is a serious health problem effecting an increasing number of person worldwide. In the present study, the aim was to investigate whether there is an association among epicardial adipose tissue thickness, insulin resistance, lymphocyte to monocyte ratio (LMR) and monocyte count-to-high density lipoprotein cholesterol ratio (MHR) levels in drug naïve patient with metabolic syndrome. Twenty-two consecutive drug-naïve women diagnosed with MetS and 30 age matched consecutive healthy women (as the control group) were recruited into the study. MHR was significantly higher [12.1 (10.5–16.4) vs 10.3 (7.0–13.8); p <0.01], whereas LMR was significantly lower in patients with MetS [3.6 (2.5–4.1) vs [4.1 (3.3–5.9) p = 0.02]. The present study shows that both LMR and MHR may be novel and useful indicators of MetS.

Keywords

Lymphocyte; Monocyte; Cholesterol; Metabolic Syndrome

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Introduction

The metabolic syndrome (MetS) or syndrome X is a serious health problem effecting an increasing number of person worldwide. Mets is defined as a co-occurrence of varied metabolic risk factors including visceral obesity, dyslipidaemia, hyperglycaemia, and hypertension [1, 2]. Epicardial adipose tissue (EAT) is a visceral fat deposit located between the heart and the pericardium. EAT acts as a metabolically active complex endocrine organ by releasing several types of molecules and hormones that have important systemic effects [3,4]. İncreased EAT may play a role in the development of both insulin resistance (IR) and cardiovascular diseases (CVDs) as potentially causes local inflammation and likely has direct effects on coronary atherosclerosis [5]. Because of the EAT thickness or volume is an independent predictor of visceral adiposity it may represent a measurable risk factor and prediction of the cardio-metabolic risk [6].

Chronic low-grade inflammation and immune cells are considered to be significant risk factors in CVDs. It has been demonstrated a positive correlation between inflammatory markers and IR in previous studies [2, 7].

Increased monocyte count or activity and lower high-density lipoprotein cholesterol (HDL-C) levels and monocyte count-to-high density lipoprotein cholesterol ratio (MHR) have been associated with inflammation [8-10]. The lymphocyte to monocyte ratio (LMR) is another novel systemic inflammatory marker that can be easily calculated from complete blood count [9].

In the present study, the aim was to investigate whether there is an association among EAT thickness, insulin resistance, LMR and MHR levels in patient with metabolic syndrome.

Material and Method

This case–control study was conducted at the Yüksek Ihtisas Education and Research Hospital, Ankara, Turkey between April and December 2016. The study approved by the local Institutional Review and all of the participants gave informed consent. The universal principles of the Helsinki Declaration were applied throughout the study.

Twenty-two consecutive drug-naïve women diagnosed with MetS and 30 age and body mass index (BMI) matched consecutive healthy women (as the control group) were recruited into the study. None of the patients and the controls had any sign or symptom of infection during investigation.

The diagnosis of MetS was based on the National Cholesterol Education Program Adult Treatment Panel III update criteria [11] of 3 or more of the 5 features of 1) central obesity (waist circumference [WC] ≥88 cm for women); 2) elevated triglycerides (≥150 mg/dl); 3) diminished high-density lipoprotein (HDL) cholesterol (<50 mg/dl for women); 4) systemic hypertension (systolic blood pressure ≥130 or diastolic blood pressure ≥85 mm Hg); and 5) elevated fasting glucose (≥100 mg/dl). Exclusion criteria were as following: smoking, any lung, autoimmune disease or connective tissue disease, chronic kidney and/or liver disease, peripheral vascular disease, and, coronary artery disease, cardiomyopathy or decompensated heart failure, and any malignancy.

Initial evaluation included a thorough physical examination; blood pressure measurement, basal hematological and biochemical profile, fasting blood glucose (FBG), fasting insulin (FI), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and serum lipid levels. All subjects' height, weight, and WC were measured, and body mass index (BMI) was calculated. WC was measured to the nearest 0.5 cm on bare skin between the tenth rib and the iliac crest. All cases and controls underwent standard ECG and transthoracic echocardiography using a Vivid 7 (GE Pro/Expert) machine with a 3.5 MHz transducer. Epicardial fat thickness was measured on the right ventricular free wall in at least two locations, from both parasternal longitudinal and transverse parasternal views in systole [4]. Fasting blood samples were obtained from the antecubital vein early in the morning.

MHR values was calculated by dividing the absolute monocyte count by the HDL-C level. LMR was calculated as a simple ratio of the absolute lymphocyte count to the monocyte absolute count. Homeostatic model assessment of insulin resistance (HOMA- IR) index was calculated using the following formula: FG (mg/dl) × FI level (μU/ml) / 405. All of the other blood analyses were carried out within two hours of blood sampling, using a hematology analyzer (GEN-S; Beckman-Coulter Inc., Brea, CA) at the central laboratories of the hospital. The age, BMI, blood pressure, and, basal hematological and biochemical profile, FBG, FI, HbA1c, AST, ALT, LMR and MHR levels of each participant were recorded.

Statistical Analysis

Statistical analysis was performed using SPSS version 18 (Statistical Package for the Social Sciences, Chicago, IL). The data were summarized as mean ± standard deviation and median (minimum–maximum). The Kolmogorov-Smirnov test was used to determine normal distribution of all quantitative data. Student's t test or Mann Whitney U test was used for group comparisons. Correlations among LMR, MHR and other variables were assessed using Pearson or Spearman correlation coefficient along with related p values. A chi-square test was performed for nominal or ordinal variables between groups, where appropriate. Statistical test and correlation coefficient was chosen according to whether the data distribution is normal or not. P values less than 0.05 were accepted as significant.

Results

Twenty-two consecutive women who had MetS and met all inclusion criteria were enrolled into the study as study group. For the control group, 30 healthy, consecutive women matched for age and BMI were recruited within the same time interval. Demographic and laboratory data of the groups were presented in the Table 1.

WC, blood pressure levels, fasting blood glucose, total and LDL cholesterol levels were significantly higher in the study group than in the control group (Table 1).

MHR and CRP levels of the patients with MetS were found to be statistically significantly higher than the control group ($p < 0.001$). LMR values were significantly lower in the MetS group than in the control group ($p < 0.004$).

Echocardiography results of the groups were shown in the Table 2. EFT levels were higher in the Mets group when compared the control ($p=0.01$).

Pearson's correlation analysis revealed a significant negative correlation between LMR level and EFT (r=-0.485, p= 0.039) and a significant positive correlation between MHR level and EFT (r= 0.600, p= 0.011) in the patients with MetS.

Table 1. Demographic and laboratory data of the groups.

Parameter	MetS+ group (n=22)	Control group (n=30)	p value
Age (years)	55.4± 3.1	53.6± 2.6	0.66
BMI (kg/m^2)	31 (23± 5.4)	30 (16.4± 7.2)	0.71
Waist circumference	109 (18± 4.1)	86 (8± 5.2)	0.01
Systolic BP (mmHg)	152 (110-155)	130 (100-150)	0.05
Diastolic BP (mmHg)	90 (60-95)	80 (65-90)	0.03
FBG (mg/dl)	105± 33	89± 23	0.03
Hemoglobin (g/dl)	14.1± 3.6	13± 4.4	0.39
Fasting insulin, µU/ml	16± 5.4	9,3± 4.1	0.02
HOMA-IR	4.8± 2.6	1.8± 2.6	0.01
Creatinine (mg/dl)	0.78± 0.19	0.80± 0.22	0.95
HbA1c, %	6.1 (5.8- 7.1)	4.9 (3.5- 5.4)	0.01
Total cholesterol (mg/dL)	201± 33	183± 32	0.71
LDL- cholesterol (mg/dL)	166± 41	125± 38	0.30
HDL- cholesterol (mg/dL)	45± 21	55± 20	0.07
Triglyceride (mg/dL)	179± 35	116± 78	0.01
AST (IU/L)	39 (14- 79)	35 (19- 45)	0.44
ALT (IU/L)	44 (13- 55)	22 (16- 44)	0.71
C-reactive protein (mg/L)	6.6 (3.9- 5.2)	4.2 (2.4- 5)	0.03
WBC X 10^3	8.1± 4.6	6.8± 1.6	0.07
LMR	3.6 (2.5–4.1	4.1 (3.3–5.9)	0.02
MHR	12.1(10.5–16.4)	10.3 (7.0–13.8)	0.01

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase BMI: body mass index, BP: blood pressure, FPG, fasting plasma glucose, HDL: High-density lipoprotein, HbA1c: hemoglobin A1c, LDL: Low-density lipoprotein, LMR: lymphocyte to monocyte ratio, MHR: monocyte count-to-high density lipoprotein cholesterol ratio. Data are presented as mean± SD.

Table 2. Echocardiography results of the groups.

Parameter	MetS + group (n=22)	Control group (n=30)	p value
HR, beat/min	77.4± 10.3	78.2± 9.6	0.66
LVEF, %	61.8± 1.7	61.5± 2.9	0.77
LVEDD (mm)	45.3± 5.1	46.5± 4.3	0.60
LVESD (mm)	26.7± 3.5	29.7± 2.9	0.82
EFT (mm)	6.1± 1.7	4.81± 2.1	0.01

EFT- Epicardial Fat Thickness, HR-heart rate, LVEDD-left ventricular end-diastolic diameter, LVEF- left ventricular ejection fraction, LVESD-left ventricular end-systolic diameter. Data are presented as mean± SD.

Discussion

Association of inflammation, monocytes and atherogenesis is a well-known entity. Inflammation has been widely considered as a critical factor in the pathogenesis of atherosclerosis and CVD. MetS has been recognized as a pro-inflammatory state associated with elevated levels of the pro-inflammatory markers [12]. In spite a lack of specificity for the cause of inflammation, it has been demonstrated an important association between elevated serum concentrations of C-reactive protein an inflammation marker and the prevalence of underlying CVDs. Moreover, certain treatments that reduce coronary artery disease risk also limit inflammation [13].

Lymphocyte values reduce in inflammatory status as a response to stress hormones, and this is associated with poor prognosis in cardiovascular disease. Activation of monocytes plays a critical role in chronic inflammation and atherosclerosis, and monocytes and transformed macrophage cells trigger the production of other inflammatory cytokines [14]. The first steps in formation of atherosclerosis is accumulation, oxidation and glycation of LDL in the endothelial intima. Monocyte chemoattractant protein 1 that promotes the chemotaxis of monocytes is produced by the endothelium in response to oxidized LDL and other stimuli. Then monocytes differentiate into macrophages and these macrophages start to phagocytes of oxidized LDL and become foam cells [15, 16].

Previous studies have been associated with the severity of coronary artery disease and low LMR and high MHR has been regarded as a surrogate marker for endothelial dysfunction and inflammation [17, 18]. In this study, first time in the literature, drug naïve MetS patient's value of the LMR and MHR were compared the healthy age and BMI matched ones. The study confirmed that LMR values were significantly lower and MHR values were significantly higher in the patients with Mets and they may be useful indicators of MetS.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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